REMARKS

Claim 13, as amended, and claims 14-17 are pending in the instant application. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

1. Rejection of claims 13-15 under 35 U.S.C. § 112, first paragraph

The Office Action maintains a rejection of claims 13-15 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that claims 13-15 do not limit the functional attributes of the encompassed molecules, and that one of ordinary skill in the art would reasonably conclude that claims 13-15 are not limited to compositions of matter that bind AGP-3 or APRIL. The Action also states that claims 13-15 encompass a genus of molecules that is highly variant in function because the claims do not require that the molecules bind to AGP-3 or APRIL.

Applicants respectfully disagree with the Action's assertion that the specification does not contain an adequate written description of the claimed invention. However, in an effort to expedite prosecution of the pending claims to allowance, Applicants have amended claim 13 to recite that "the composition of matter is a specific binding partner for AGP-3 or APRIL." Applicants reserve the right to pursue claims lacking the above limitation in a timely filed continuation or divisional application. Applicants submit that amended claim 13 (from which claims 14-15 directly or indirectly depend) satisfies the written description requirement of 35 U.S.C. § 112, first paragraph, and respectfully request that this ground of rejection be withdrawn.

2. Rejections of claims 13-15 under 35 U.S.C. § 103(a)

The Office Action maintains a rejection of claims 13-15 under 35 U.S.C. § 103(a), as being unpatentable over International Publication No. WO 98/39361 (the '361 publication) in view of International Publication No. WO 99/11791 (the '791 publication). Applicants' understanding of the asserted teachings of the '361 and '791 publications is fully set forth in Applicants' response to the Office Action mailed December 1, 2004. The instant Action concludes that it would have been

prima facie obvious at the time the claimed invention was made to substitute a polypeptide comprising residues 33-104 for the complete extracellular domain in the fusion proteins disclosed in the '361 publication, and that one of ordinary skill in the art would be motivated to do so by the disclosure in the '361 publication that a recombinant form of the extracellular portion of TACI acts to intercept the normal endogenous ligands which bind TACI and the disclosure in the '791 publication that "cysteine repeat regions of members of the TNF-receptor family [are] ***important*** for ligand binding" (emphasis added). The instant Action also concludes that one of ordinary skill in the art would expect that a polypeptide which is shorter than the complete extracellular domain of TACI would be able to intercept exogenous ligands which activate the native TACI receptor provided that the polypeptide comprises the cysteine rich regions identified in the '791 publication as being ***important*** in ligand binding.

The Office Action also maintains a rejection of claims 13-15 under 35 U.S.C. § 103(a), as being unpatentable over U.S. Patent No. 6,475,987 (the '987 patent) in view of the '791 publication. Applicants' understanding of the asserted teachings of the '987 patent and '791 publication is fully set forth in Applicants' response to the Office Action mailed December 1, 2004. The instant Action concludes that it would have been *prima facie* obvious at the time the claimed invention was made to substitute a polypeptide comprising the cysteine-rich repeats of the BCMA extracellular domain in the fusion protein comprising the immunoglobulin Fc domain disclosed in the '987 patent, and that one of ordinary skill in the art would be motivated to do so by the disclosure in the '791 publication that "cysteine repeat regions of members of the TNF-receptor family [are] ***important*** for ligand binding" (emphasis added). The instant Action also concludes that one of ordinary skill in the art would expect that a polypeptide which is shorter than the complete extracellular domain of BCMA would function in an assay to identify compounds which bind to the extracellular portion of BCMA.

Applicants respectfully disagree with the Action's assertion that either the '361 and '791 publications in combination or the '987 patent and the '791 publication in combination render the claimed invention obvious. Critical to both obviousness rejections is the Action's assertion that the '791 publication discloses that "cysteine repeat regions of members of the TNF-receptor family [are] ***important*** for ligand binding" (emphasis added). However, while the '791 publication states that the "cysteine rich regions, which are motifs of approximately 40 amino acids with about 6 cysteines, are ***involved*** in ligand binding" (at page 7, lines 27-29; emphasis added), the '791 publication simply

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does not disclose that the cysteine repeat regions are ***important*** – let alone sufficient – for ligand binding. Applicants contend that absent the teachings of the instant specification, one of ordinary skill in the art would not recognize that the cysteine repeat regions are ***sufficient*** for ligand binding, and therefore, would not substitute a polypeptide comprising residues 33-104 for the complete extracellular domain in the fusion proteins disclosed in the '361 publication or the '987 patent.

Moreover, the '791 publication's lone phrase that the "cysteine rich regions . . . are involved in ligand binding" (again, not that such regions are important or sufficient) must be weighed against all of the reference's other teachings. Applicants contend that the instant Action's focus on this single statement in the '791 publication (as well as the elevation of the role of such regions from "involved" to "important," and the additional implication that such regions are sufficient) contravenes the requirements of M.P.E.P. § 2141.02, which states that "[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." Applicants contend that when the '791 publication is considered in its entirety as required under M.P.E.P. § 2141.02, this reference clearly equates the ***entire*** extracellular domain with ligand binding, and therefore, does not lead to the use of the cysteine-rich pseudo-repeats alone.

The instant Action appears to overlook the fact that the '791 publication is replete with disclosure which gives meaning to the term "involved in ligand binding." For example, when the '791 publication refers to the "ligand binding domain" or "soluble active fragment," it refers ***not*** to the cysteine-rich pseudo-repeats, but rather, to the ***entire*** extracellular domain (*see* page 1, lines 22-23; page 9, lines 15-17; page 29, lines 22-23; page 69, line 30; page 78, line 18; and page 121, line 24). The '791 publication states that:

> In one embodiment, the invention provides a soluble active fragment of an AP04 polypeptide. Such ***a soluble active fragment includes the ligand binding domain*** of an AP04 polypeptide ***and can be***, for example, ***a truncated polypeptide encoding the extracellular domain*** of an AP04 polypeptide.

(page 25, lines 6-11) (emphasis added). The '791 publication also states that:

> In one embodiment, the invention provides ***a soluble AP06 active fragment that includes an AP06 ligand binding domain***. A soluble AP06 active fragment ***can be***, for example, ***a truncated polypeptide encoding the extracellular domain*** of an AP06 polypeptide.

(page 29, lines 7-11) (emphasis added). However, the '791 publication ***never*** defines the "ligand binding domain" or a "soluble active fragment" as constituting the cysteine-rich

pseudo-repeats ***alone***. If the '791 publication intended to disclose that the cysteine repeat regions are sufficient for ligand binding, then clearly the '791 publication would have defined the "ligand binding domain" or "soluble active fragment" as constituting the cysteine repeat regions, or alternatively, would have used the terms "ligand binding domain," "soluble active fragment," and "cysteine repeat regions" interchangeably.

More telling than the '791 publication's failure to equate ligand binding with the cysteine repeat regions alone, however, is what the applicant sought to claim in the '791 publication. While a review of the '791 publication's 43 claims shows that the applicant included a claim to an "active fragment [that] is an AP04 ***extracellular*** ligand binding domain" (claim 9; page 125; emphasis added), the applicant included not a single claim to an active (or ligand binding) fragment comprising only the cysteine-rich pseudo-repeats of the extracellular domain. Surprisingly, the applicant neglected to add the latter claim despite the fact that there is no surcharge for inclusion of additional claims in International applications. Clearly, if the applicant of the '791 publication believed that the cysteine-rich pseudo-repeats constitute the ligand binding domain, the applicant would have claimed an active fragment comprising the portion of the extracellular domain of AP04 that contains only the cysteine-rich pseudo-repeat domains. Instead, the applicant of the '791 publication claimed the entire extracellular ligand binding domain. Applicants contend that by disclosing that the ligand binding domain constitutes the entire extracellular domain, and claiming only the entire extracellular domain, the '791 publication ***as a whole*** actually discloses that in addition to the cysteine rich regions, other undefined portions of the extracellular domain are necessary for ligand binding. Thus, absent Applicants' teachings, one of ordinary skill in the art, reading the '791 publication, would use the entire extracellular domain.

The M.P.E.P. sets forth a number of ways in which Applicants can argue that an improper rationale has been used for combining references in an obviousness rejection (*see* M.P.E.P. § 2145(X)). Applicants contend that in rejecting claims 13-15 as being unpatentable over either the '361 and '791 publications or the '987 patent and the '791 publication, the Action uses improper hindsight, applies an improper obvious to try rationale, and discounts the fact that the '791 publication teaches away from the claimed invention. As described above, while the '791 publication contains the lone statement that "cysteine rich regions . . . are involved in ligand binding," the '791 publication repeatedly discloses (as well as claims) the entire extracellular domain

as the ligand binding domain. Thus, when the Action asserts that the '791 publication discloses that the cysteine repeat regions are important (or even sufficient) for ligand binding, the Action is invariably relying on the disclosure in Applicants' specification, and therefore, is using improper hindsight reasoning. In addition, if the Action means to suggest that one of ordinary skill in the art, having read the '791 publication, would attempt to delineate the precise portions of the extracellular domain that are necessary and sufficient for ligand binding by creating and testing all possible fragments of the extracellular domain (even those including the cysteine rich regions), such an expectation would constitute an application of an improper obvious to try rationale. Finally, by disclosing that the ligand binding domain refers to the entire extracellular domain, the '791 publication actually teaches away from the use of the cysteine rich regions alone. Applicants contend, therefore, that one of ordinary skill in the art, reading the '791 publication, would not use the cysteine rich regions alone, but rather would use the entire extracellular domain, and if desirous of using a portion of the extracellular domain, would attempt to identify the minimal portion required for ligand binding from among numerous possibilities.

Applicants respectfully contend that rejections based on 35 U.S.C. § 103(a) have been traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Canella believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
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